REMARKS

In response to the Office Action dated January 16, 2002, applicants hereby elect, with traverse, Group V, claims 1, 6-9, 21-28 and 61 drawn to SEQ ID NO: 9, the nucleic acid molecule encoding human Bim$_{EL}$.

Request for Withdrawal of Restriction Between Group V and Group X

Under the rules of the PCT, it is improper to restrict between a protein and an encoding polynucleotide. Accordingly, applicants request rejoinder of Group X, claims 10, 15-20, 51 and 60 drawn to protein SEQ ID NO: 10, with its coding sequence, SEQ ID NO: 9. (Applicants note that in the Office Action, SEQ ID NO: 7 incorrectly is indicated as the coding sequence for SEQ ID NO: 10. Applicants elect Group X with the understanding that it is the Group which reads on SEQ ID NO: 9.)

Applicants contend that the Examiner's finding of lack of unity of invention is improper. The Examiner has stated that there is no unity of invention among the claims because of the lack of a technical feature that defines a contribution over the prior art. To evidence a lack of a technical feature, the Examiner references a 1995 publication for disclosing a nucleic acid molecule that encodes "beta tubulin which is a non-apoptosis inducing polypeptide and is thus a derivative of a polypeptide having one or more identifying characteristics of Bim in that it encodes a polypeptide that comprises numerous fragments of SEQ ID NO: 2." To refute this finding of the Examiner's, applicants attached hereto a clustal protein alignment, between Bim$_{EL}$ of (SEQ ID NO: 10) and ß tubulin, indicating that only 40 of the 198 amino acids are identical, *i.e.* there is less than 20% identity, which generally is regarded as insubstantial. Moreover, applicants have amended claims 1 and 10 to recite, "the characteristics [.... ability to induce apoptosis," thereby further distinguishing over beta tubulin as the Examiner has admitted that beta tubulin is non-apoptosis inducing.

In conclusion, applicants request, at the very least, examination of Groups V and X together, in compliance with the rules of the PCT.

Request for Withdrawal of Restriction Between Groups V and Groups I-IV

The Examiner's restriction of Groups I-IV, dividing each polynucleotide into a separate invention, is in violation of MPEP §803.04, which states that "***normally*** ten (10) sequences constitute a reasonable number for examination purposes." This is true even if each nucleotide sequence is an independent and distinct invention under 35 USC §121. The Commissioner has decided *sua sponte* to waive the requirements of 37 CFR §1.141 *et seq.* and to permit the claiming of a reasonable number of nucleotide sequences in an application, thereby to "aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office." Automatically restricting every single polynucleotide into a separate applicantions will unduly burden applicants in the field of biotechnology, and is contrary to the letter and spirit of the Commissioner's *sua sponte* waiver of 37 CFR §1.141 *et seq.*

Groups I-V recite five polynucleotide sequences, and applicants request that all sequences be examined together because they can be examined without undue burden and they are related. Groups I-V respectively recited the polynucleotide sequences for murine Bims, Bim$_L$, Bim$_{EL}$ and human Bim$_L$ and Bim$_{EL}$.

At the very least, applicants request examination of the *human* Bim$_{EL}$ and Bim$_L$ nucleic acid sequences. Bim$_{EL}$ and Bim$_L$ are different isoforms of the Bim molecule, and are closely related because they have the same function and effect. Moreover, their structure is similar in that Bim$_L$ is essentially a truncated version of Bim$_L$

Applicants also request examination of murine Bims, Bim$_L$ and Bim$_{EL}$ polynucleotides with human Bim$_L$ and Bim$_{EL}$ molecules. Again, these molecules are closely related isoforms of two different species. Their structure is very similar: human and mouse Bim$_{EL}$ molecules exhibit up to 89% homology.

In conclusion, at the very least, examination of the human Bim$_{EL}$ and Bim$_L$ nucleic acid sequences is requested. Applicants further request examination of murine Bims, Bim$_L$ and Bim$_{EL}$ polynucleotides. An examination of five polynucleotide sequences is a reasonable number and well within the Commissioner's *sua sponte* waiver of requirements of 37 CFR §1.141 *et seq.*

Request for Withdrawal of Restriction Between Groups X and Groups VI-IX

For the reasons given above, applicants request withdrawal of the restriction between Groups VI-X, drawn to respectively to murine Bims, BimL, BimEL and human BimL and BimEL. Applicants contend that these Groups are related because they are structurally similar isoforms that are capable of being used together.

Request for Withdrawal of Restriction Between Groups V or X and Groups XI-XXII

Applicants traverse the restriction between Groups V or X and Groups XI-XXII on the grounds that Groups XI-XXII are method claims for using the novel compositions of Groups V or X and therefore under the *Ochiai* guidelines, restriction is improper.

Election of Species of Item 6

Applicants traverse the election of species between claims 19 and 20 because searching both the heterodimer and the homodimer of the protein would not be an undue burden and the Examiner has brought forth no evidence that the heterodimer and the homodimer would have different effects. Applicants elect the homodimer of claim 19 for initial examination.

Election of Species of Item 7

Applicants traverse the election of species required in Item 7 because the Examiner has misunderstood claim 22. All the variant claims are directed to molecules which do not bind or couple with the dynein light chain. Claim 22 *does not* recite a molecule which positively binds the dynein light chain. Rather, claim 22 further defines the non-dynein binding molecule of claim 21 in terms of the specific mutation which prevents binding to the dynein light chain occurring in the region of the polypeptide which would normally bind the dynein light chain. The Examiner has misunderstood the variant molecule claims in relation to the issue of dynein light chain binding. Accordingly, claim 22 should be examined along with claims 21 and 23.

Election of Mutation

Applicants traverse the election of species required in Items 8-10 because searching both the mutated nucleic acid molecules would not be an undue burden and the Examiner has brought forth no evidence that the mutants would have different effects. Applicants elect the substitution D51G of claims 23-26 and claims 31-34 for initial examination.

Conclusion

Receipt of the initial Office Action on the merits is awaited. Applicants, reserve the right to file a divisional application covering the non-elected subject matter.

Respectfully submitted,

July 16, 2002
Date

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

Marked-Up Version of the Claims

1. (Amended Once) A nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide having one or more of the identifying characteristics of Bim or a derivative or homologue thereof**, wherein the characteristic is the ability to induce apoptosis**.

10. (Amended Once) A polypeptide comprising the amino acid sequence of Bim or having one or more of the identifying characteristics thereof or derivative or homologue thereof**, wherein the characteristic is the ability to induce apoptosis**.

ATTACHMENT A

CLUSTAL PROTEIN ALIGNMENT

[EBI Banner]

Your ClustalW Results:

Use JalView:

Pairwise Scores:

CLUSTAL W (1.81) Multiple Sequence Alignments

Sequence format is Pearson
Sequence 1: ACtub 443 aa
Sequence 2: BimEL 198 aa
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score: 14
Guide tree file created:
[/net/nfs0/vol1/production/w3nobody/tmp/794269.614141-443121.dnd]
Start of Multiple Alignment
There are 1 groups
Aligning...
Group 1: Delayed
Sequence:2 Score:1559
Alignment Score 97
CLUSTAL-Alignment file created
[/net/nfs0/vol1/production/w3nobody/tmp/794269.614141-443121.aln]

Your Multiple Sequence Alignment:

794269.614141-443121.aln

CLUSTAL W (1.81) multiple sequence alignment

```
ACtub           MREIVHLQTGQCGNQIGAAFWQTISGEHGLDSNGVYNGSSELQLERMSVYASGNKYVPRA 60
BimEL           MAKQPSDVSSECD-----------------------------------REGRQLQPAE 23
                *  :     :.:*.                                      .*.:  *

ACtub           VLVDLEPGTMDAVRAGPFGQLFRPDNFVFGQSGAGNNWAKGHYTEGAELVDNVLDVVRRE 120
BimEL           RPPQLRPGAPTSLQTEPQGNPEG------NHGGEGDSCPHGSPQG---------------- 62
                   :*.**:  :::: * *:          .:.* *:. .:*

ACtub           AEGCDCLQGFQITHSLGGGTGAGMGTLLISKIREEFPDRMMATFSVVPSPKVSDTVVEPY 180
BimEL           ----------PLAPPASPGPFATRSPLFIFMRRSSLLSRSSSGY---------------- 96
                          :: . . *. *  ..*:*   *..: .*  : :

ACtub           NATLSVHQLVEHSDETFCIDNEALYDICMRTLKLSNPSYGDLNYLVSAVMSGVTTCLRFP 240
BimEL           --------------FSFDTDRSPAPMSCDKSTQTPSPPCQAFNHYLSAMAS--------- 133
                             :*  *...    * :: : ..*.   :*: :**: *

ACtub           GQLNSDLRKLAVNMVPFPRLHFFMVGFAPLTSRGAHSFRAVSVPELTQQMFDPKNMMAAS 300
BimEL           ------------------------------------MRQAEPADMRPEIW--------- 147
                                                    :* .. .::  :::

ACtub           DFRNGRYLTCSAIRGKVAMKEVEDQMRNVQSKNSSYFVEWIPNNIQTALCAIPPRGLKMS 360
BimEL           ------------------------------------------------------------
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ACtub           STFIGNSTSIQELPKRVGEQFTAMFRRKAFLHWYTG-EGMDEMEFTEAESNMNDLVSEYQ 419
BimEL           ---------IAQELRRIGDEFNAYYARRVFLNNYQAAEDHPRMVILRLLRYIVRLVWRMH 198
                         * : ::*:*::*.* : *:.**: * . *.  .* : .    :  ** . :

ACtub           QYQDAGIDEEEEEYEEELPLEGEE 443
BimEL           ------------------------
```

Your guide tree:

794269.614141-443121.dnd

```
(ACtub:0.42929,BimEL:0.42929);
```
